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AF/B

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

1634

Applicants: Arguello *et al.*

Appl. No.: 09/077,615

Filing Date: October 23, 1998

Title: METHODS FOR SEPARATING AND/OR IDENTIFYING DNA MOLECULES

Docket No.: 028979-0103

Commissioner for Patents
Washington, D.C. 20231

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Atty. Dkt. No. 028979-0103

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Rafael ARGUELLO *et al.*

Title: METHODS FOR SEPARATING AND/OR IDENTIFYING DNA MOLECULES

Appl. No.: 09/077,615

Filing Date: 10/23/1998

Examiner: J. C. Einsmann

Art Unit: 1634

#35

BRIEF ON APPEAL

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This brief is in furtherance of the Notice of Appeal filed in this case on October 8, 2002. The required fee for filing an appeal brief, as set forth in 37 C.F.R. § 1.17(c) is included in our Check No. 730443. Any fee deficiency may be charged, or overpayment credited to, Deposit Account No. 50-2350. This brief is transmitted in triplicate and in conformance with the other requirements of 37 C.F.R. §1.192(a).

I. REAL PARTY IN INTEREST

Pel-Freez Clinical Systems, LLC, a Wisconsin Limited Liability Company of Brown Deer, Wisconsin is the real party in interest in this appeal.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF CLAIMS

Claims 55-69 and 73-76 remain pending in this application and were finally rejected in the Office Action of July 8, 2002. All of these claims are on appeal. A copy of the appealed claims is contained in Appendix A. Claims and 1-54 and 70-72 have been cancelled and are not on appeal.

IV. STATUS OF AMENDMENTS

No Amendments after Final have been filed by Appellants.

V. SUMMARY OF THE INVENTION

Appellant's invention provides methods for identifying a DNA molecule. Specification page 1, lines 3-4. The methods involve hybridizing a single-stranded DNA molecule with a complementary reference strand of DNA to form a test duplex which is separated from at least one control duplex. Page 9, lines 9-14. The positions to which the test duplex and control duplex are detected, and the position of the test duplex is assigned an exact numerical migration value. Page 24, lines 23-32. The single-stranded DNA molecule is identified by matching the exact numerical migration value of the test duplex with a migration value in database containing the migration values of identified DNA molecules that is independent or separate from the separation. Page 24, lines 5-11 and 25-26, FIGS. 1 and 9-15.

VI. ISSUES

The issues on appeal are as follows:

1. Whether claims 55-69 and 73-76 meet the definiteness requirements of 35 U.S.C. § 112, second paragraph;

2. Whether claims 55-69 and 73-76 are nonobvious under 35 U.S.C. §103 over Zimmerman *et al.*, Nucleic Acids Research, Vol. 21, No. 19, 4541-4547 (1993), in view of Sapirstein *et al.*, Seed Science Technology 14, 489-517 (1986); and

3. Whether claims 55-69 and 73-76 are nonobvious under 35 U.S.C. §103 over Zimmerman *et al.*, in view of Sapirstein *et al.*, both further in view of Mullins *et al.*

VII. GROUPING OF THE CLAIMS

Claims 55-69 and 73-76 stand or fall together.

VIII. ARGUMENT

1. The rejection under § 112, second paragraph, is clearly in error and should be withdrawn.

In the Final Office Action dated July 8, 2002, claims 55-69 and 73-76 were "rejected under 35 U.S.C. 112, second paragraph, as being indefinite" for reciting "'wherein the database of migration values is independent of the separation' because it is not clear how this is possible." Appellants respectfully disagree with this rejection and are unsure as to how using the word "independent" in accord with it common and ordinary meaning of "separate" or "apart from" renders the claims indefinite. *See, e.g.*, The Random House Thesaurus 373 (College ed. 1991), a copy of which is enclosed. In fact, the Examiner properly interpreted the meaning of this element stating, "[f]or the purposes of examination herein, the claims have been interpreted to mean that the database must be separate from the gel used for separation of the duplexes." Because the claims apprise the skilled artisan of their meaning, Appellants respectfully request the rejection of claims 55-69 and 73-76 as indefinite be withdrawn.

As a point of clarification, Appellants also disagree with the Examiner's statements that:

> the database of migration values is intrinsically dependent upon the separation as the database is a record of the distances the test duplexes traveled in the separating step (b). Thus, it is not clear how the database can be independent from the separation. It seems that if the database were independent of the separation, the values contained in the database would be arbitrary values with no clear meaning or basis.

These statements appear to be based on a misunderstanding of the invention set forth in the claims. The present claims only recite the performance of a single separation – the separation between the test duplex and one or more control duplexes. No other separation is required to perform the claimed invention, although the performance of additional separations falls within the scope of the

claimed invention. The database is made up of "migration values of identified DNA molecules" but the claims do not require the separation of the identified DNA molecules or the calculation of their migration values be performed in the claimed separation of the test duplex from the one or more control duplexes. The migration values of the identified DNA molecules can be readily calculated from one or several separations that are not the claimed separation of the test duplex from the control duplex. As long as the migration values assigned in the different separations can be correlated to a common scale then the migration values can be easily related to on another. Thus, the database of values is not required to be "intrinsically dependent upon the (claimed) separation" or "a record of the distances the test duplexes traveled in the separating step (b)."

2. The claims are not obvious over Zimmerman *et al.* in view of Sapirstein *et al.*

In the Office Action of July 8, 2002, claims 55-59 and 73-76 were "rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman *et al.* in view of Sapirstein *et al.* (Seed Science Technology (1986) 14(3) 489-517)." This rejection is improper not only because it is a hindsight reconstruction of the claimed invention, as Sapirstein *et al.* is not analogous to the claimed invention, but also because the references fail to teach or suggest all of the elements of the claimed invention. Moreover, the references are directed to different art areas and problems and teach away from their combination.

As discussed above, the present claims are directed to methods of identifying a DNA molecule using duplex separations and database matching. Zimmerman *et al.* teach genotyping DQA1 and DQB1 alleles using DNA probe hybridization and heteroduplex analysis. Contrast these to the non-analogous teachings of Sapirstein *et al.* which relate to wheat cultivar identification based on gliadin profiles. Sapirstein *et al.* do not disclose identification of anything at the molecular level, such as protein or DNA. Sapirstein *et al.* merely distinguish wheat cultivars. In order to discriminate between wheat cultivars, Sapirstein *et al.* do not use any hybridization technique, much less DNA hybridization. Moreover, Sapirstein *et al.* only care about protein banding patterns, not the identity of any specific protein in the banding pattern. In simplistic terms, if the banding pattern of sample X matches the database banding pattern for cultivar Y, then sample X is cultivar Y. The identity or sequence of the specific proteins that make up the banding

pattern are irrelevant. Accordingly, Appellants respectfully submit that a skilled artisan attempting to identify DNA would simply not look to art dealing with wheat cultivar banding for direction, other than in hindsight.

Additionally, the combination of Zimmerman *et al.* and Sapirstein *et al.* does not state a *prima facie* case of obviousness because they do not teach or suggest all of the elements of the appealed claims. Specifically, these references fail to teach or suggest at least two steps of the claimed invention, namely "assigning an exact numerical migration value to the position to which the test duplex migrates[,]" and "identifying the DNA molecule by matching the exact migration value with a database of migration values of identified DNA molecules, wherein the database of migration values is independent of the separation."

The fact that the primary reference fails to teach or suggest these claim elements is explicitly admitted by the Examiner: "Zimmerman *et al.* do **not** assign an exact numerical migration value to the distance traveled by the heteroduplexes. Furthermore, Zimmerman *et al.* do **not** provide a database of migration values that is independent of (or separate from) the gel used in the separation step." Despite the Examiner's protests to the contrary, Zimmerman *et al.* also do not disclose a database of migration values of identified DNA molecules as required by the instant claims. To the skilled artisan a database is generally known as a "large collection of data organized especially for rapid search and retrieval (as by computer)." Merriam Webster's Collegiate Dictionary 293 (Tenth Ed. 1997), a copy of which is enclosed. To meet this definition any database would intrinsically have to be separate and apart from a physical separation performed on heteroduplexes. Thus, the skilled artisan would not consider "[t]he left side of the gel in Figure 3...to be a database of test duplex migration values" as argued by the Examiner because the left side of the gel does not contain a "large collection of data organized especially for rapid search and retrieval" nor is the database separate and apart from the physical separation assay.

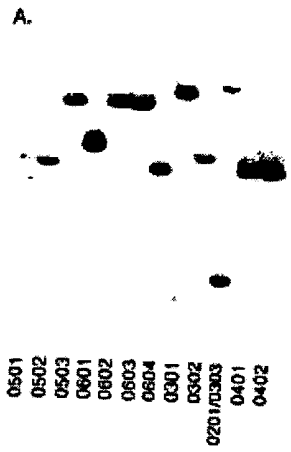
Instead, one skilled in the art would recognize the left side of the gel in figure 3 for what it is – a limited number of positive controls against which the heteroduplexes must be compared on the gel to identify the DNA molecules in the heteroduplex. In order to positively identify a truly unknown HLA allele in an individual, Zimmerman *et al.* would have to run well in excess of 100 positive controls. See Zimmerman *et al.* which note on page 4541 that the

HLA*DRB1, HLA*DQA1, HLA*DQB1, HLA*DPA1 and HLA*DPB1 genes contain 66, 10, 13, 4 and 26 separate alleles, respectively, for a grand total of 119 different alleles. These are only a fraction of the known HLA alleles which number in the hundreds, if not thousands. Schreuder *et al.*, Tissue Antigens, 58:109 (2001) (abstract enclosed). Therefore, Zimmerman *et al.* fails to teach several elements of the claimed invention.

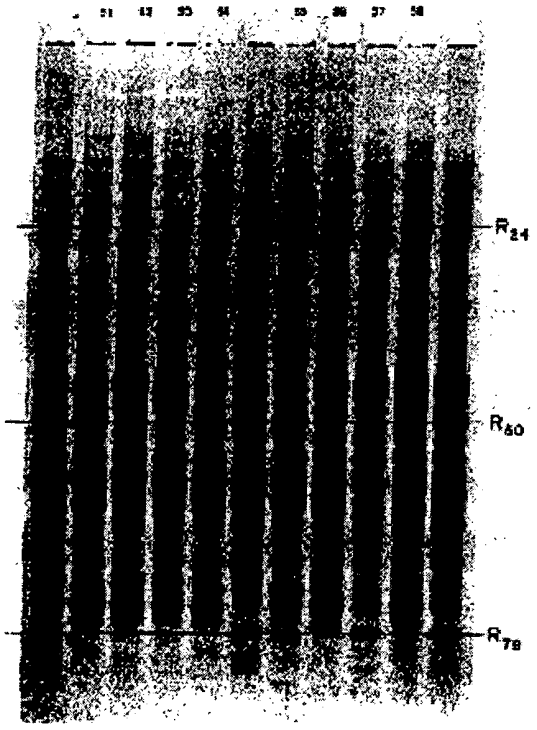
Sapirstein *et al.* do not make up for the deficiencies of Zimmerman *et al.* because Sapirstein *et al.* also fail to teach or suggest these same elements of the claimed invention, namely "assigning an exact numerical migration value to the position to which the test **duplex** migrates; and identifying the DNA molecule by matching the exact migration value with a database of migration values of identified DNA molecules..." In fact, Sapirstein *et al.* deal only with individual proteins. Sapirstein *et al.* do not bother with hybridizing proteins to form duplexes, nor are they the least bit concerned with DNA. Although Sapirstein *et al.* disclose a database of gliadin protein band migration values nowhere do they disclose that any of the specific gliadin protein bands was identified or known. Sapirstein *et al.* only care about protein banding patterns, not the identity of any specific protein in the banding pattern. It is the combination of gliadin bands, not the individual bands themselves, that is important. The identity or sequence of the specific proteins that make up the banding pattern are irrelevant.

In order to overcome the deficiency of Zimmerman *et al.*, one skilled in that art would recognize that Sapirstein *et al.* would have to disclose a method for identifying a specific protein based on its position. This Sapirstein *et al.* do not disclose, instead their complete emphasis on banding patterns is evident throughout the article. See, e.g., Summary, p. 489 "unknown (or test) electropherograms (were compared) with counterpart protein patterns[.]" Therefore, Sapirstein *et al.* cannot teach or suggest "matching the exact migration value with a database of migration values of identified DNA molecules" recited in the claimed invention, and, as Zimmerman *et al.* also fail to teach this element, the combination of these two cannot render the claimed invention obvious. Instead, Appellants respectfully submit that the Examiner has cobbled together bits and pieces of non-analogous pieces of prior art in a hindsight reconstruction of the claimed invention.

Additionally, there is no suggestion or motivation in the references to combine their teaching. The Examiner forces together a combination of non-analogous references based not upon any teaching or suggestion in the cited references, but the advantages achieved by the claimed invention. At the same time the Examiner ignores the parts of the references that teach away from their combination. For example, Zimmerman *et al.* repeatedly point out that their method is simple and provides results that are easy to interpret. See, e.g., Page 4541, bottom of right column through page 4542, top of left column ("[t]his study presents a novel PCR-based approach... to achieve accurate and simple genotyping" and "this study has employed strategic labeling... to simplify HD banding patterns"). In contrast, Sapirstein *et al.* state that "standardising (protein) band migration distances... is sufficiently **tedious to require** implementation by means of a computer." Page 492, fourth paragraph. Contrast Zimmerman *et al.* where the "resulting HD pattern is comprised of a **single** product in homozygous individuals or **two** products in heterozygous individuals[,]" page 4542, top of left column, with Sapirstein *et al.* where the banding patterns consist of a large number of protein bands, an example of which is shown below:



Zimmerman *et al.*



Sapirstein *et al.*

In fact, Sapirstein *et al.* reveal in Figures 5-8 that none of the numerous wheat cultivars studied provided a banding pattern that had less than 26 different bands. Figure 6, Pellisier cultivar.

Moreover, Sapirstein *et al.* rely on features not relevant to the teachings of Zimmerman *et al.*, such as complex statistical analysis and the subjective determination of "the intensity of the gliadin band(s)" as a "secondary feature" in the identification of wheat cultivars. Based on the divergent teachings of these references, the skilled artisan simply would not look to the complex, unrelated method of Sapirstein *et al.* for wheat cultivar identification to modify the simplified procedure of Zimmerman *et al.* for human lymphocyte typing.

In summary, not only is Sapirstein *et al.* not analogous to the claimed invention, the improper combination of Zimmerman *et al.* and Sapirstein *et al.* do not teach or suggest all elements of the claimed invention. Moreover, there is no suggestion or motivation other than hindsight to combine the references as suggested by the Examiner. In reality, a careful reading of the references reveals they teach away from their combination. Therefore, the rejection of the claims as being obvious over Zimmerman *et al.* and Sapirstein *et al.* should be withdrawn.

3. The claims are not obvious over Zimmerman *et al.* and Sapirstein *et al.* both in view of Mullins *et al.*

Claims 55-69 and 73-76 were also "rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman *et al.* in view of Sapirstein *et al.* (Seed Science Technology (1986) 14(3) 489-517) both further in view of Mullins *et al.*" The teachings of Zimmerman *et al.* and Sapirstein *et al.* are discussed above. Mullins *et al.* were cited by the Examiner "merely to demonstrate that it was known in the art at the time the invention was made to determine exact numerical mobility values for heteroduplex nucleic acid molecules."

However, the teachings of Mullins *et al.* are irrelevant to the claimed invention because they do not calculate the exact migration distance of a single DNA duplex as the Examiner contends. Instead, in example 4 of Mullins *et al.* cited by the Examiner, migration values "were calculated as the <u>average distance</u> of migration of the <u>**two** heteroduplex bands</u> divided by the distance of migration of the homoduplex bands." Page 50, line 37 through page 51, line 2. Because the migration values are based on an "<u>average</u> distance of <u>**two**</u> heteroduplex bands" the

migration value relates to both of these heteroduplexes and is not specific for either one of them. Thus, any migration value calculated in Mullins *et al.* is simply not capable of providing for the positive and actual identification of any of the DNA molecules in the heteroduplex bands as is required by the claimed invention. Moreover, because Mullins *et al.* are cited solely for the proposition that mobility values of heteroduplexes can be measured this reference must also fail to overcome the deficiencies of Zimmerman *et al.* and Sapirstein *et al.* discussed above. Therefore, the rejection of the claims as being obvious over Zimmerman *et al.* and Sapirstein *et al.* both in view of Mullins *et al.* should be withdrawn.

IX. CONCLUSION

For the foregoing reasons, Appellants submit that Claims 55-69 and 73-76 are patentable over the cited references, and that the final rejection of these claims should be reversed.

Respectfully submitted,

Date December 6, 2002

By _____

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APPENDIX A - CLAIMS ON APPEAL

55. A method for identifying a DNA molecule comprising:

(a) hybridizing a single strand DNA molecule with a complementary reference DNA strand to form a test duplex;

(b) separating the test duplex from at least one control duplex run in the same separation;

(c) detecting the positions to which the test duplex and the at least one control duplex migrate in the separation;

(d) assigning an exact numerical migration value to the position to which the test duplex migrates; and

(e) identifying the DNA molecule by matching the exact migration value with a database of migration values of identified DNA molecules, wherein the database of migration values is independent of the separation.

56. The method of claim 55 wherein the complementary reference DNA strand is labeled.

57. The method of claim 55 further comprising repeating steps (a)— (e) one or more times wherein a different complementary reference strand is utilized in each repeat of steps (a)-(e) to identify the DNA molecule.

58. The method of claim 55 wherein step (b) comprises gel electrophoresis.

59. The method of claim 55 wherein the database of migration values comprises migration values of alleles of a gene selected from the group consisting of HLA, TAP, LMP, ras, non-classical HLA and Bf.

60. The method of claim 55 wherein the database of migration values comprises migration values for mammalian MHC genes.

61. The method of claim 59 wherein the alleles are selected from the group consisting of HLA alleles.

62. The method of claim 60 wherein the DNA molecule comprises a portion of an HLA gene.

63. The method of claim 55 further comprising confirming the identity of the DNA molecule by sequencing the test duplex, performing sequence specific primer amplification analysis on the test duplex or performing sequence specific oligonucleotide analysis on the test duplex.

64. The method of claim 55 wherein the method can resolve a difference of one, two or three nucleic acid positions between the DNA molecule and the complementary sequence of the complementary reference DNA strand.

65. The method of claim 55 wherein the DNA molecule and complementary reference DNA strand have the same number of nucleotides.

66. The method of claim 55 wherein the complementary reference DNA strand consists of the wild type sequence of a naturally occurring DNA strand of interest or a naturally occurring mutant thereof.

67. The method of claim 55 wherein the at least one control duplex comprises (i) duplexes which have faster and slower mobility than the test duplex or (ii) duplexes which have graded mobilities.

68. The method of claim 55 wherein the identified DNA molecule is matched to a second identified DNA molecule and the method is used to match tissue between a prospective tissue donor and a prospective tissue recipient.

69. The method of claim 55 further comprising amplifying the DNA molecule prior to step (a).

73. A method for identifying a DNA molecule, comprising:

(a) amplifying a DNA molecule to produce amplified double stranded DNA molecules;

(b) denaturing the amplified double stranded DNA molecules into single stranded DNA molecules wherein the single stranded DNA molecules include sense and antisense strands;

(c) hybridizing the single stranded DNA molecules with reference DNA strands which are complementary to the single stranded DNA molecules to form test duplexes;

(d) separating the test duplexes from at least one control duplex run in the same separation;

(e) detecting the positions to which the test duplexes and the at least one control duplex migrate in the separation;

(f) assigning an exact numerical migration value to the position to which the test duplex migrates; and

(g) identifying the DNA molecule by matching the exact migration with a database of migration values of identified DNA molecules, wherein the database of migration values is independent of the separation.

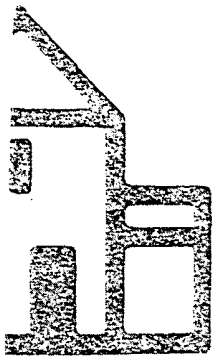
74. The method of claim 73 wherein the reference DNA strands are labeled.

75. The method of claim 73 further comprising repeating steps (a)-(g) one or more times wherein a different complementary reference strand is utilized in each repeat of steps (a)-(g) to identify the DNA molecule.

76. The method of claim 73 wherein step (f) comprises:

(i) assigning a migration value to the at least one control duplex; and

(ii) assigning the exact numerical migration value to the test duplex based on the relative migration position of the test duplex compared to the migration value of the control duplex.



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apart, as a matter of fact, to tell
ıonest, in point of fact, actually,
vn to it.
j. The new man is an indefat-
nd will go far: tireless, inex-
evering, persistent, diligent,
c, sedulous, unfaltering, unflag-
ıwearying, staunch.
1 The indefensible village fell
hours: unable to withstand at-
defenseless; open to attack, un-
ıable, vincible. 2 *Her purchase*
was an indefensible waste of
ible, beyond justification, unjus-
cable, unpardonable, without
ıle; open to criticism, improper,

e, invincible, invulnerable, pro-
ible, justifiable, excusable, par-
ible, rational, tenable.
The store will be closed for an
d: unspecified, having no fixed
ined, indeterminate, unknown,
it; illimitable, measureless, lim-
im an indefinite answer: unset-
indistinct, vague; not clearly de-
efined, amorphous, indecisive,
ve, obscure, ambiguous, unsure.
e, clear-cut, certain, limited,
2 definite, certain, settled, sure,

The book left an indelible
ne. The ink made an indelible
rmanent, unforgettable, lasting,
manently fixed, fast, ineradica-
:, unremovable, incapable of
ır wiped out, ingrained, deep-

His indelicate manners are the
ıgh upbringing: coarse, crude,
unbecoming; clumsy, awkward.
ndelicate story to tell in mixed
ısive, lacking good taste, indis-
; unrefined; off-color, immodest,
, vulgar, suggestive, indecorous,
oad, obscene, coarse, gross, im-

:e, refined, seemly, decorous,
polished. 2 decent, chaste, re-
ıroper.
he company indemnified him
r his car: reimburse, repay, pay
ıte, requite, remunerate, recom-
ght, make restitution, make up
l, rectify, make amends, satisfy,

1 *You can identify some trees*
ıtions of the leaves. The map
us indentations along the shore-
ı, incision, cavity, furrow, score;
ity, niche, pocket, bay, inset. 2

High heels made indentations in the linoleum: dent, pit, gouge, depression, nick.
Ant. bump, protruberance, projection, prominence.

independence *n. The American colonies won their independence from England:* emancipation, liberty, freedom, self-determination, self-government, freedom from control, sovereignty, self-reliance, liberation, autonomy.
Ant. dependence; subordination, subjection; servitude, slavery, bondage; reliance, dependency.

independent *adj.* 1 *Children should be encouraged to be independent thinkers:* self-reliant, uncontrolled, on one's own, autonomous, free, self-directing, individualistic, uncoerced; unconstrained, free from the control or influence of others. 2 *The United States became an independent country in 1776:* free, self-governing, autonomous; self-determining, sovereign. 3 *The medical college is independent of the university:* separate, not joined to or associated with, unattached to, distinct from, exclusive, apart from, unconnected with, unallied. 4 *The inheritance made him independent for life:* solvent, well-to-do, well-off, in easy circumstances, well-fixed, affluent, *Informal* well-heeled.
Ant. 1 dependent; influenced, controlled, directed; subordinate, subject, tributary, subservient, servile, slavish, subject, attached, interrelated. 4 dependent, reliant, beholden, attached.

indescribable *adj. The artistry of Michelangelo's* Pietà *is indescribable:* beyond description, inexpressible, beyond words, ineffable, beggaring description; indefinable; overwhelming, unutterable.

indestructible *adj. Toys for toddlers should be as indestructible as possible:* unbreakable, damage-resistant, infrangible, enduring, permanent, everlasting, imperishable, incapable of being destroyed.
Ant. destructible, perishable, breakable, unenduring, fragile, frangible.

indeterminate *adj. The acting superintendent will serve for an indeterminate time:* unspecified, undetermined, unstipulated, uncertain, unfixed in extent or amount, unclear, obscure, not clear, unresolved, vague, undefined; ambiguous, problematic, perplexing, indefinite.
Ant. specified, precise, definite, clear, certain, determined, fixed, defined.

index *n.* 1 *The poems are given in the index by author:* alphabetical list, catalog, register, glossary. 2 *Overeating is often an index of emotional stress:* sign, token, indication, indicator, symptom, clue, evidence, manifestation, proof, mark.

indicate *v.* 1 *The patient's pallor indicates anemia:* be a sign of, be symptomatic of, show, designate, denote, imply, point to, suggest; evince, bespeak, reveal, symbolize, signify, stand for, mean, represent. 2 *Indicate where the pain is with your finger:* point out, point to, specify, direct attention to. 3 *A barometer indicates air pressure:* show, make known, register, reveal, tell, establish, record.

indication *n. There was no indication this morning that it would rain:* sign, hint, intimation, signal, manifestation, token, warning, evidence, mark, clue, suggestion, foretoken, hint, symptom, gesture, demonstration; portent, augury, omen, boding, foreboding, premonition, presage; signifying, telling, indicating, designation, mention, showing, pointing.

indicative *adj. Fever may be indicative of infection:* suggestive, indicatory, characteristic, evidential, symptomatical, symptomatic, expressive, significant, emblematic, symbolic, representative, denotative, connotative, designative.

indict *v. The grand jury indicted him for embezzlement:* arraign, accuse, charge, inculpate, criminate, impute, bring to justice, cite, impeach, prosecute; find an indictment against, prefer charges, have up, pull up, bring up.

indifference *n.* 1 *He would have preferred anger to her cold indifference:* unconcern, absence of feeling, lack of interest, disinterest, neglect, inattention, impassiveness, impassivity, nonchalance, aloofness, carelessness, negligence, insensibility, insensitivity, disdain, insouciance, apathy, coldness. 2 *Religion is a matter of indifference to many of today's youth:* unimportance, triviality, no import, insignificance, paltriness, inconsiderableness.
Ant. 1 concern, warmth, sensibility; attention, interest, eagerness, caring. 2 importance, magnitude, significance, greatness.

indifferent *adj.* 1 *The writer was indifferent to criticism, good or bad:* unconcerned, not caring, insensible, without interest, impervious, uninterested, insusceptible, detached, unmindful, impassive, unmoved, insouciant, apathetic, nonchalant, cool, aloof. 2 *The actor's indifferent performance left the audience cold:* perfunctory, mediocre, not very good, undistinguished, uninspired, ordinary, so-so, rote, commonplace, neither good nor bad, medium, middling, fair, modest, moderate, passable, average, betwixt and between; falling short of any standard of excellence, second-rate, rather poor.
Ant. 1 avid, eager, keen, agog; interested, sensitive, susceptible, caring, sympathetic, responsive, compassionate, enthusiastic. 2 choice, notable, remarkable, exceptional, rare, first-class, superior, excellent, fine.

indigenous *adj. Cotton is indigenous to the southern United States:* native, growing naturally, aboriginal, originating in, characteristic of, endemic, homebred, home-grown, domestic, autochthonous.
Ant. naturalized; exotic; foreign, alien, extraneous, imported.

indigent *adj. Many indigent people receive government aid:* needy, destitute, in want, lack-

Merriam-Webster's Collegiate® Dictionary

TENTH EDITION

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Springfield, Massachusetts, U.S.A.

-est (1792) 1 : of, relating to, or suggestive of very good : FIRST-RATE (a ~ place to stay)
-i-zəm\ *n* (1819) 1 : the style or conduct of ...y and artistic style of the latter part of the 19th ...rtificiality and excessive refinement
Dan. fr. ON *Danr*] (14c) 1 : a native or inhabitant ...erson of Danish descent 3 : GREAT DANE
...d\ *n, often cap* (bef. 12c) : an annual tax believed ...d orig. to buy off Danish invaders in England or to ...ppose them but continued as a land tax
... *n* (bef. 12c) 1 : the law in force in the part of ... : Danes before the Norman Conquest 2 : the part ...e Danelaw
...hemism] (1797) : DAMN 4
(14) : DAMNED
n [ME *daunger*, fr. OF *dangier*, alter. of *dongier*, ... *iniarium*, fr. L *dominium* ownership] (13c) 1 ... ON b *obs* : REACH, RANGE 2 *obs* : HARM, DAMAGE ... lity to injury, pain, harm, or loss (a place where ... without ~) 4 : a case or cause of danger (the ...
haic : ENDANGER
...ə-rəs; 'dān-jərs, -zhrəs\ *adj* (15c) 1 : exposing to ... 2 : able or likely to inflict injury or harm — **dan-ger-ous-ness** *n*
HAZARDOUS, PRECARIOUS, PERILOUS, RISKY mean bring... the chance of loss or injury. DANGEROUS applies to ...ay cause harm or loss unless dealt with carefully (*dangerous* mission). HAZARDOUS implies great and ca... urm or failure (claims that smoking is *hazardous* to ...CARIOUS suggests both insecurity and uncertainty ...us living by gambling). PERILOUS strongly implies the ...ger (*perilous* mountain roads). RISKY often applies to ...pted danger (shied away from *risky* investments).
vb **dan-gled; dan-gling** \-g(ə-)liŋ\ [prob. of Scand. ...a *dangle* to dangle] *vi* (ca. 1590) 1 : to hang loosely ...be able to swing freely 2 : to be a hanger-on or a ... occur in a sentence without having a normally ex... ...lation to the rest of the sentence (the word *climbing* ...nountain the cabin came into view" is *dangling*) ~ ... dangle : SWING 2 a : to keep hanging uncertain... ...an inducement — **dan-gler** \-g(ə-)lər\ *n*
1 : the action of dangling 2 : something that ...
also 'da-n²l\ *n* [Heb *Dānī'ēl*] 1 : the Jewish hero ... ...d who as an exile in Babylon interprets dreams, ...lyptic visions, and is divinely delivered from a ... ...of narratives, visions, and prophecies in ... ...ian Scripture — see BIBLE table
n, pl **da-ni-os** [NL, genus name] (ca. 1889) : any ... ...ntly colored Asian cyprinid fishes
...\ *adj* (14c) : of, relating to, or characteristic of Da... or the Danish language
1 : the Germanic language of the Danes 2 *pl* Da... ...anish pastry
(ca. 1928) : a pastry made of a rich raised dough
[ME *danke*] (1573) : unpleasantly moist or wet *syn* ... **ly** *adv* — **dank-ness** *n*
r, dän-\ *n* [F, fr. *danser* to dance] (1828) : a ...
...ēr; dän-'sə(r)z, dän-'süz\ *n* [F, fem. of *danseur*] (1829) ...lancer
...tē-ən, 'dän-\ *n* (ca. 1850) : a student or admirer of

t, Dao-is-tic *var of* TAOISM, TAOIST, TAOISTIC
...\ *n* [NL, genus name, fr. L, laurel, fr. Gk *daphnē*] ... genus (*Daphne*) of Eurasian shrubs of the mezereon ...dous flowers whose colored calyx resembles a corolla
...\ *n* [L, fr. Gk *Daphnē*] : a nymph who is transformed ... to escape the pursuing Apollo
...ē-ə\ *n* [NL, genus name] (1847) : any of a genus ...nute freshwater branchiopod crustaceans with thin ...sed as locomotive organs — compare WATER FLEA
...əs\ *n* [L, fr. Gk] : a Sicilian shepherd renowned ... ...y as the inventor of pastoral poetry
...\ *adj* [ME *dapyr*, fr. MD *dapper* quick, strong; akin to ...vy, OCS *debelŭ* thick] (15c) 1 a : neat and trim ... excessively spruce and stylish 2 : alert and lively ...anners — **dap-per-ly** *adv* — **dap-per-ness** *n*
...\ *n* [ME *dappel-gray*, adj., gray marked with spots of ... 1580) 1 : any of numerous usu. cloudy and rounded ... of a color or shade different from their background ... state of being dappled 3 : a dappled animal
pled; dap-pling \-p(ə-)liŋ\ *vt* (1599) : to mark with ... to produce a dappled pattern (*sun dappling* through ...
...p-ple *adj* (15c) : marked with small spots or patches ... the background (a ~ fawn)
...ən\ *n* [*diamine* + *phenyl* + *sulfone*] (1952) : an anti... $C_{12}H_{12}N_2O_2S$ used esp. against leprosy
...an \,där-bē-ən-'jōn\ *n* [prob. fr. *Darby & Joan*, comic ...song] (1857) : a happily married usu. elderly couple
(ca. 1885) : DARDIC
...ən\ *adj or n* [L *Dardanus*, fr. Gk *Dardanos*] (1600) ...
...ər-'dā-nē-ən\ *adj* (1596) : TROJAN
...ik\ *n* (1910) : a complex of Indic languages spoken ... of the Indus
... *vb* **dared; dar-ing; dares** *or (auxiliary)* **dare** [ME ... ing. pres. indic.), fr. OE *dear*; akin to OHG *gitar* (1st & ...ndic.) dare, Gk *tharsos* courage] (bef. 12c) *verbal auxiliary* ...ficiently courageous to (no one *dared* say a word) (... lf love —G. B. Shaw) ~ *vi* : to have sufficient courage ...) ~ *vt* 1 a : to challenge to perform an action esp. as a proof of courage (*dared* him to jump) b : to confront boldly : DEFY (*dared* the anger of his family) 2 : to have the courage to contend against, venture, or try (the actress *dared* a new interpretation of this classic role) — **dar-er** \'dar-ər, 'der-\ *n*
²dare *n* (1594) 1 : an act or instance of daring : CHALLENGE (foolishly took a ~) 2 : imaginative or vivacious boldness : DARING
²dare-dev-il \'dar-ˌde-vᵊl, 'der-\ *n* (1794) : a recklessly bold person — **dare-dev-il-ry** \-vᵊl-rē\ *n* — **dare-dev-il-try** \-vᵊl-trē\ *n*
²daredevil *adj* (1832) : recklessly and often ostentatiously daring *syn* see ADVENTUROUS
dareful *adj* (1605) *obs* : DARING
daren't \'dar-ənt, 'der-\ : dare not : dared not
dare-say \,dar-'sā, ,der-\ *vt* (13c) : venture to say : think probable — used in pres. 1st sing. ~ *vi* : AGREE, SUPPOSE — used in pres. 1st sing.
¹dar-ing *adj* (1582) : venturesomely bold in action or thought *syn* see ADVENTUROUS — **dar-ing-ly** \-iŋ-lē\ *adv* — **dar-ing-ness** *n*
²daring *n* (1651) : venturesome boldness
Dar-jee-ling \där-'jē-liŋ\ *n* [*Darjeeling*, India] (1907) : a tea of high quality grown esp. in the mountainous districts of northern India
¹dark \'därk\ *adj* [ME *derk*, fr. OE *deorc*; akin to OHG *tarchannen* to hide] (bef. 12c) 1 a : devoid or partially devoid of light : not receiving, reflecting, transmitting, or radiating light b : transmitting only a portion of light 2 a : wholly or partially black b *of a color* : of low or very low lightness 3 a : arising from or showing evil traits or desires : EVIL (the ~ powers that lead to war) b : DISMAL, GLOOMY (had a ~ view of the future) c : lacking knowledge or culture 4 : not clear to the understanding 5 : not fair in complexion : SWARTHY 6 : SECRET (kept his plans ~) 7 : possessing depth and richness (a ~ voice) 8 : closed to the public (the theater is ~ in the summer) *syn* see OBSCURE — **dark-ish** \'där-kish\ *adj* — **dark-ly** *adv* — **dark-ness** *n*
²dark *n* (13c) 1 : a : a place or time of little or no light : NIGHT, NIGHTFALL b : absence of light : DARKNESS 2 : a dark or deep color — in the dark 1 : in secrecy (most of his dealings were done *in the dark*) 2 : in ignorance (kept the public *in the dark* about the agreement)
dark *vi* (14c) *obs* : to grow dark ~ *vt* : to make dark
dark adaptation *n* (1909) : the phenomena including dilation of the pupil, increase in retinal sensitivity, shift of the region of maximum luminosity toward the blue, and regeneration of visual purple by which the eye adapts to conditions of reduced illumination — **dark-adapted** \,därk-ə-'dap-təd\ *adj*
dark age *n* (1730) 1 : a time during which a civilization undergoes a decline as a *pl, cap D&A* : the European historical period from about A.D. 476 to about 1000; *broadly* : MIDDLE AGES b *often pl, often cap D&A* : the Greek historical period of three to four centuries from about 1100 B.C. 2 a *often pl, often cap D&A* : the primitive period in the development of something (in the 1890s, way back in baseball's *Dark Ages* —R. W. Creamer) b *often pl, often cap D&A* : a state of stagnation or decline
dark-en \'där-kən\ *vb* **dark-ened; dark-en-ing** \'där-kə-niŋ\ *vi* (14c) 1 : to grow dark : become obscured 2 : to become gloomy ~ *vt* 1 : to make dark 2 : to make less clear : OBSCURE (the financial crisis ~ed the future of the company) 3 : TAINT, TARNISH 4 : to cast a gloom over 5 : to make of darker color — **dark-en-er** \-kə-nər\ *n*
dark field *n* (1865) : the dark area that serves as the background for objects viewed in an ultramicroscope
dark-field microscope *n* (1926) : ULTRAMICROSCOPE
dark horse *n* (1831) 1 a : a usu. little known contender (as a racehorse) that makes an unexpectedly good showing b : an entrant in a contest that is judged unlikely to succeed 2 : a political candidate unexpectedly nominated usu. as a compromise between factions
dark lantern *n* (1650) : a lantern that can be closed to conceal the light
dark-le \'där-kəl\ *vi* **dark-led; dark-ling** \-k(ə-)liŋ\ [back-formation fr. *darkling*] (1800) 1 a : to become clouded or gloomy b : to grow dark 2 : to become concealed in the dark
dark-ling \'där-kliŋ\ *adv* [ME *derkelyng*, fr. *derk* dark + *-lyng* -ling] (15c) : in the dark
²dark-ling *adj* (1739) 1 : DARK 2 : done or taking place in the dark
darkling beetle *n* (1816) : TENEBRIONID
dark matter *n* (1982) : nonluminous matter not yet directly detected by astronomers that is hypothesized to exist because the visible matter in the universe is insufficient to account for various observed gravitational effects
dark reaction *n* (1927) : any of a series of chemical reactions in photosynthesis not requiring the presence of light and involving the reduction of carbon dioxide to form carbohydrate; *also* : CALVIN CYCLE
dark-room \'därk-ˌrüm, -ˌrum\ *n* (1841) : a room with no light or with a safelight for handling and processing light-sensitive photographic materials
dark-some \'därk-səm\ *adj* (ca. 1530) : gloomily somber : DARK
darky or dark-ie \'där-kē\ *n, pl* **darkies** (1775) : a black person — usu. taken to be offensive
¹dar-ling \'där-liŋ\ *n* [ME *derling*, fr. OE *dēorling*, fr. *dēore* dear] (bef. 12c) 1 : a dearly loved person 2 : FAVORITE
²darling *adj* (1509) 1 : dearly loved : FAVORITE 2 : very pleasing : CHARMING — **dar-ling-ly** \-liŋ-lē\ *adv* — **dar-ling-ness** *n*
darn \'därn\ *vb* [perh. fr. F dial. *darner*] *vt* (ca. 1600) 1 : to mend with interlacing stitches 2 : to embroider by filling in with long running or interlacing stitches ~ *vi* : to do darning — **darn-er** *n*
²darn *n* (1720) : a place that has been darned (a sweater full of ~s)
³darn *adj or adv* [euphemism] (1781) : DAMNED
⁴darn *vb* (1781) : DAMN — **darned** \'därn(d)\ *adj or adv*
⁵darn *n* (1840) : DAMN
dar-nel \'där-nᵊl\ *n* [ME] (14c) : any of several usu. weedy grasses (genus *Lolium*)
darning needle *n* (1761) 1 : a long needle with a large eye for use in darning 2 : DRAGONFLY, DAMSELFLY
dart \'därt\ *n* [ME, fr. MF, of Gmc origin; akin to OHG *tart* dart, OE *daroth*] (14c) 1 a *archaic* : a light spear b (1) : a small missile usu. with a pointed shaft at one end and feathers at the other (2) *pl but sing* in concr. : a game in which darts are thrown at a target 2 a : something projected with sudden speed; *esp* : a sharp glance b : something causing sudden pain or distress (~s of sarcasm) 3 : something with a slender pointed shaft or outline; *specif* : a stitched tapering fold in a garment 4 : a quick movement (made a ~ for the door)
²dart *vt* (1580) 1 : to throw with a sudden movement 2 : to thrust or move with sudden speed 3 : to shoot with a dart containing a usu. tranquilizing drug ~ *vi* : to move suddenly or rapidly (~ed across the street)
dart-board \'därt-ˌbōrd, -ˌbȯrd\ *n* (1901) : a usu. circular board (as of compressed bristles) used as a target in the game of darts
dart-er \'där-tər\ *n* (1813) 1 : ANHINGA 2 : any of numerous small American freshwater bony fishes (esp. genera *Ammocrypta, Etheostoma*, and *Percina* of the family Percidae)
Dar-win-i-an \där-'wi-nē-ən\ *adj* (1860) : of or relating to Charles Darwin, his theories esp. of evolution, or his followers — **Darwinian** *n*
Dar-win-ism \'där-wə-ˌni-zəm\ *n* (1864) : a theory of the origin and perpetuation of new species of animals and plants that offspring of a given organism vary, that natural selection favors the survival of some of these variations over others, that new species have arisen and may continue to arise by these processes, and that widely divergent groups of plants and animals have arisen from the same ancestors; *broadly* : biological evolutionism — **Dar-win-ist** \-wə-nist\ *n or adj*
Darwin's finches \där-wənz-\ *n pl* [Charles *Darwin*] (1947) : finches of a subfamily (Geospizinae) having great variation in bill shape and confined mostly to the Galapagos islands
Darwin tulip \,där-wən-\ *n* (1889) : a tall late-flowering tulip with the flowers single and of one color
¹dash \'dash\ *vb* [ME *dasshen*] *vt* (13c) 1 : to break by striking or knocking 2 : to knock, hurl, or thrust violently 3 : SPLASH, SPATTER 4 a : RUIN, DESTROY (the news ~ed his hopes) b : DEPRESS, SADDEN c : to make ashamed 5 : to affect by mixing in something different (his delight was ~ed with bitterness over the delay) 6 : to complete, execute, or finish off hastily — used with *down* or *off* (~ed down a drink) (~ off a letter) 7 [euphemism] : ¹DAMN 4 ~ *vi* 1 : to move with sudden speed (~ed through the rain) 2 : SMASH
²dash *n* (14c) 1 a *archaic* : BLOW b (1) : a sudden burst or splash (2) : the sound produced by such a burst 2 a : a stroke of a pen b : a punctuation mark — that is used esp. to indicate a break in the thought or structure of a sentence 3 : a small usu. distinctive addition (a ~ of salt) (a ~ of humor) 4 : flashy display 5 : animation in style and action 6 a : a sudden onset, rush, or attempt b : a short fast race 7 : a long click or buzz forming a letter or part of a letter (as in Morse code) 8 : DASHBOARD 2
dash-board \'dash-ˌbōrd, -ˌbȯrd\ *n* (1846) 1 : a screen on the front of a usu. horse-drawn vehicle to intercept water, mud, or snow 2 : a panel extending across the interior of a vehicle (as an automobile) below the windshield and usu. containing dials and controls
dashed \'dasht\ *adj* (ca. 1839) : made up of a series of dashes
da-sheen \da-'shēn, də-\ *n* [origin unknown] (ca. 1899) : TARO
dash-er \'da-shər\ *n* (1790) 1 : a dashing person 2 : one that dashes; *specif* : a device having blades for agitating a liquid or semisolid
dashi \'dä-(ˌ)shē\ *n* [Jp, broth] (ca. 1961) : a fish broth made from dried bonito
da-shi-ki \də-'shē-kē, dä-, da-\ *n* [modif. of Yoruba *dáṣíkí*] (ca. 1968) : a usu. brightly colored loose-fitting pullover garment
dash-ing *adj* (1796) 1 : marked by vigorous action : SPIRITED (a ~ young horse) 2 : marked by smartness esp. in dress and manners — **dash-ing-ly** \-iŋ-lē\ *adv*
dash-pot \'dash-ˌpät\ *n* (1861) : a device for cushioning or damping a movement (as of a mechanical part) to avoid shock
das-sie \'da-sē\ *n* [Afrik] (1736) : HYRAX
das-tard \'das-tərd\ *n* [ME] (15c) 1 : COWARD 2 : a person who acts treacherously or underhandedly
das-tard-ly \-lē\ *adj* (1576) 1 : COWARDLY 2 : characterized by underhandedness or treachery (a ~ attack) (a ~ villain) *syn* see COWARDLY — **das-tard-li-ness** *n*
da-ta \'dā-tə, 'da- *also* 'dä-\ *n pl but sing or pl in constr, often attrib* [L, pl. of *datum*] (1646) 1 : factual information (as measurements or statistics) used as a basis for reasoning, discussion, or calculation (the ~ is plentiful and easily available —H. A. Gleason, Jr.) (comprehensive ~ on economic growth have been published —N. H. Jacoby) 2 : information output by a sensing device or organ that includes both useful and irrelevant or redundant information and must be processed to be meaningful 3 : information in numerical form that can be digitally transmitted or processed
usage *Data* leads a life of its own quite independent of *datum*, of which it was originally the plural. It occurs in two constructions: as a plural noun (like *earnings*), taking a plural verb and plural modifiers (as *these, many, a few*) but not cardinal numbers, and serving as a referent for plural pronouns (as *they, them*); and as an abstract mass noun (like *information*), taking a singular verb and singular modifiers (as *this, much, little*), and being referred to by a singular pronoun (*it*). Both constructions are standard. The plural construction is more common in print, evidently because the house style of several publishers mandates it.
data bank *n* (1966) : DATABASE
da-ta-base \'dā-tə-ˌbās, 'da- *also* 'dä-\ *n* (ca. 1962) : a usu. large collection of data organized esp. for rapid search and retrieval (as by a computer)
data processing *n* (1954) : the converting of raw data to machine-readable form and its subsequent processing (as storing, updating, combining, rearranging, or printing out) by a computer — **data processor** *n*
data structure *n* (1963) : any of various methods of organizing data items (as records) in a computer
¹date \'dāt\ *n* [ME, fr. OF, ultim. fr. L *dactylus* — more at DACTYL] (14c) 1 : the oblong edible fruit of a palm (*Phoenix dactylifera*) 2 : the tall palm with pinnate leaves that yields the date

eness an individual, activity, or object possesses

: the range of permissible energy values that are
ssible for an atom can have and still be associ-
be used to form bonds — compare CONDUCTION

923) : a single electron or one of two or more
ell of an atom that is responsible for the chemi-
m

ə-ˈlen-ch(ē-)ə, -len(t)-sē-ə\ *n* [*Valencia*, Spain]
: of a juicy thin-skinned cultivar grown in the
ncia

en(t)-sē-ˈen(z), ˌva-lən-sē-\ *n* [*Valenciennes*,
obbin lace

ISV, fr. L *valent-*, *valens*] 1 : having a (speci-
; (*bivalent*) (*multivalent*) 2 : having (so many)
r homologous chromosomes (*univalent*)
\ *n* (15c) 1 : a sweetheart chosen or compli-
e's Day 2 a : a gift or greeting card sent
St. Valentine's Day; *esp* : a greeting card
ing (as a movie or piece of writing) expressing
tion : TRIBUTE

Valentine Day *n* (1668) : SAINT VALENTINE'S

(1852) : a salt or ester of valeric acid
n [ME, fr. MF or ML; MF *valeriane*, fr. ML
. of *valerianus* of Valeria, fr. *Valeria*, Roman
t of Pannonia] (14c) 1 : any of a genus
Valerianaceae, the valerian family) of perennial
ssess medicinal properties 2 : a drug consist-
k and roots of the garden heliotrope (*Valeriana*
d as a carminative and sedative
k-, -ˈler-\ *n* [*valerian*; fr. its occurrence in the
: any of four isomeric fatty acids $C_5H_{10}O_2$ or a
liquid acid of disagreeable odor obtained from
tically and used esp. in organic synthesis
va-ˈlā\ *n* [MF *vaslet*, *varlet*, *valet* young noble-
vant, fr. (assumed) ML *vassellittus*, dim. of ML
at VASSAL] (1567) 1 a : a man's male servant
services (as taking care of clothing) b : an
d or a public facility) who performs personal
2 : a device (as a rack or tray) for holding
cts

e as a valet
)va-ˌlā-də-ˈshā°brˇ\ *n. pl* **va-lets de chambre**
valet] (1646) : VALET 1a

: a service that provides parking of motor vehi-

a-lə-ˌtü-dᵊn-ˈer-ē-ən, -ˌtyü-\ *n* [L *valetudinaria*
lin-, *valetudo* state of health, sickness, fr. *valēre*
more at WIELD] (1703) : a person of a weak or
: one whose chief concern is being or becoming

'13) : of, relating to, or characteristic of a vale-
UK

ˌ\-ē-ə-ˌni-zəm\ *n* (1839) : the condition or
dinarian

ᵊtu-ˌer-ē, -ˈtyü-\ *adj* [L *valetudinarius*] (1581)

ies (1665) : VALETUDINARIAN

IL, fr. L, bowlegged] (1884) : of, relating to, or
ich an anatomical part is turned outward away
body to an abnormal degree ⟨~ deformity of

lso väl-ˈhä-\ *n* [G & ON; G *Walhalla*, fr. ON
slain, fr. *valr* the slain (akin to OE *wæl* slaugh-
all; akin to OE *heall* hall] : the great hall in
: the souls of heroes slain in battle are received

n (15c) : VALOR

(15c) : VALOR

[ME *valiaunt*, fr. MF *vaillant*, fr. OF, fr. pp.
, fr. L *valēre* to be strong — more at WIELD]
acting with bravery or boldness : COURAGEOUS
d by, exhibiting, or carried out with courage or
⟨~ feats⟩ — **val·iant·ly** *adv* — **val·iant·ness**

ant person
F or ML; MF *valide*, fr. ML *validus*, fr. L
) 1 : having legal efficacy or force; *esp* : ex-
gal authority and formalities ⟨a ~ contract⟩ 2
stifiable : being at once relevant and meaning-
gically correct ⟨a ~ argument⟩ ⟨~ inference⟩
nd in view : EFFECTIVE ⟨every craft has its own
'axxon : conforming to accepted principles of
ication — **va·lid·i·ty** \və-ˈli-də-tē, və-\ *n* —
y

ENT, CONVINCING, TELLING mean having such
ious attention and usu. acceptance. VALID im-
y objective truth or generally accepted author-
xeing absent⟩ ⟨a *valid* marriage⟩. SOUND implies
oming or of solid grounds ⟨a *sound* proposal for
). COGENT may stress either weight of sound
: or lucidity of presentation ⟨the prosecutor's
over the jury⟩. CONVINCING suggests a power to
osition, or reluctance to accept ⟨a *convincing*
reform⟩. TELLING stresses an immediate and
at the heart of a matter ⟨a *telling* example of

vt **-dat·ed; -dat·ing** (1648) 1 a : to make
nt official sanction to by marking c : to con-
lection); *also* : to declare (a person) elected 2
rate on a sound or authoritative basis ⟨experi-
: hypothesis⟩ *syn* see CONFIRM

ral-i-də-tion \ ˈdā-shən\ *n* (ca. 1656) : an act, process, or instance
of validating; e- .ne determination of the degree of validity of a mea-
suring device

va-line \ˈvā-ˌlēn, ˈvā-\ *n* [ISV, fr. *valeric (acid)*] (1907) : a crystalline
essential amino acid $C_5H_{11}NO_2$ that is one of the building blocks of
plant and proteins

va-lise \və-ˈlēs\ *n* [F, fr. It *valigia*] (1615) : SUITCASE

Val-ium \ˈva-lē-əm, ˈval-yəm\ *trademark* — used for a preparation of
diazepam

val-kyr-ie \val-ˈkir-ē *also* val-ˈkī-rē, ˈval-kə-rē\ *n* [G & ON; G *Wal-
küre*, fr. ON *valkyrja*, lit., chooser of the slain; akin to OE *wælcyrige*
witch, ON *valr* the slain, OHG *kiosan* to choose — more at CHOOSE]
: any of the maidens of Odin who choose the heroes to be slain in bat-
tle and conduct them to Valhalla

val-late \ˈva-ˌlāt\ *adj* [L *vallatus*, pp. of *vallare* to surround with a wall,
fr. *vallum* wall, rampart — more at WALL] (1878) : having a raised edge
surrounding a depression ⟨~ papillae of the tongue⟩

val-lec-u-la \və-ˈle-kyə-lə, və-\ *n, pl* **-u-lae** \-kyə-ˌlē, -ˌlī\ [NL, fr. LL,
little valley, dim. of L *valles* valley — more at VALE] (1859) : an ana-
tomical groove, channel, or depression; *esp* : one between the base of
the tongue and the epiglottis — **val-lec-u-lar** \-lər\ *adj*

val-ley \ˈva-lē\ *n, pl* **valleys** [ME *valey*, fr. OF *valee*, fr. *val* valley —
more at VALE] (14c) 1 a : an elongate depression of the earth's sur-
face usu. between ranges of hills or mountains b : an area drained by
a river and its tributaries 2 : a low point or condition 3 a : HOL-
LOW, DEPRESSION b : the place of meeting of two slopes of a roof that
form on the plan a reentrant angle

valley fever *n* [fr. its prevalence in the San Joaquin valley of Califor-
nia] (1938) : COCCIDIOIDOMYCOSIS

Va-lois \ˈva-ˌwä, val-ˈ\ *adj* [Philippe de *Valois* (Philip VI of France)]
(ca. 1888) : of or relating to the French royal house that ruled from
1328 to 1589

val-o-nia \və-ˈlō-nē-ə, -nyə\ *n* [It *vallonia*, fr. MGk *balanidia*, pl. of
balanidion, dim. of Gk *balanos* acorn — more at GLAND] (1722) : dried
acorn cups esp. from a Eurasian evergreen oak (*Quercus macrolepis* syn.
Q. aegilops) used in tanning or dressing leather

val-or \ˈva-lər\ *n* [ME, fr. MF *valour*, fr. ML *valor* value, valor, fr. L
valēre to be strong — more at WIELD] (15c) : strength of mind or spirit
that enables a person to encounter danger with firmness : personal
bravery

val-o-rize \ˈva-lə-ˌrīz\ *vt* **-rized; -riz·ing** [Pg *valorizar*, fr. *valor* value,
price, fr. ML] (ca. 1906) : to enhance or try to enhance the price, value,
or status of by organized and usu. governmental action ⟨using subsi-
dies to ~ coffee⟩ — **val-o-ri-za-tion** \ˌva-lə-rə-ˈzā-shən\ *n*

val-or-ous \ˈva-lə-rəs\ *adj* (15c) : VALIANT — **val-or-ous-ly** *adv*

val-our \ˈva-lər\ *chiefly Brit var of* VALOR

val-po-li-cel-la \ˌväl-pō-lə-ˈche-lə, ˌval-\ *n, often cap* [*Valpolicella*, dis-
trict in northern Italy] (1903) : a dry red Italian table wine

Val-sal-va maneuver \val-ˈsal-və-\ *n* [Antonio Maria *Valsalva* †1723
Ital. anatomist] (1886) : the process of making a forceful attempt at
expiration while holding the nostrils closed and keeping the mouth
shut for the purpose of testing the patency of the eustachian tubes or of
adjusting middle ear pressure — called also *Valsalva*

waltz \wȯls\ *n* [F, fr. G *Walzer* — more at WALTZ] (1796) : WALTZ; *specif*
: a concert waltz

val-u-able \ˈval-yə-bəl, -yə-wə-bəl\ *adj* (1589) 1 a : having monetary
value b : worth a good price 2 a : having desirable or esteemed
characteristics or qualities ⟨~ friendships⟩ b : of great use or service
(~ advice) — **val-u-able-ness** *n* — **val-u-ably** \-blē\ *adv*

valuable *n* (ca. 1775) : a usu. personal possession (as jewelry) of rela-
tively great monetary value — usu. used in pl.

valuable consideration *n* (1638) : an equivalent or compensation
having value that is given for something acquired or promised (as
money or marriage) and that may consist either in a benefit accruing to
one party or a loss falling upon the other

val-ue \ˈval-(ˌ)yü\ *vt* **-ued; -u·ing** (1873) : to place a value on
: APPRAISE

val-u-a-tion \ˌval-yə-ˈwā-shən\ *n* [MF, fr. *valuer* to value, fr. *value*]
(1529) 1 : the act or process of valuing; *specif* : appraisal of property
2 : the estimated or determined market value of a thing 3 : judgment
or appreciation of worth or character — **val-u-a-tion-al** \-shnəl, -shə-
nᵊl\ *adj* — **val-u-a-tion-al-ly** *adv*

val-u-a-tor \ˈval-yə-ˌwā-tər\ *n* (1731) : one that valuates; *specif* : one
that appraises

val-ue \ˈval-(ˌ)yü\ *n* [ME, fr. MF, fr. (assumed) VL *valuta*, fr. fem. of
valutus, pp. of L *valēre* to be worth, be strong — more at WIELD] (14c)
1 : a fair return or equivalent in goods, services, or money for some-
thing exchanged 2 : the monetary worth of something : marketable
price 3 : relative worth, utility, or importance ⟨a good ~ at the price⟩
⟨the ~ of base stealing in baseball⟩ ⟨had nothing of ~ to say⟩ 4 a : a
numerical quantity that is assigned or is determined by calculation or
measurement ⟨let *x* take on positive ~s⟩ ⟨a ~ for the age of the earth⟩
b : precise significance ⟨~ of a word⟩ 5 : the relative duration of a
musical note 6 a : relative lightness or darkness of a color : LUMI-
NOSITY b : the relation of one part in a picture to another with respect
to lightness and darkness 7 : something (as a principle or quality)
intrinsically valuable or desirable ⟨sought material ~s instead of hu-
man ~s⟩—W. H. Jones⟩ 8 : DENOMINATION 2 — **val-ue-less** \-(ˌ)yü-
ləs, -yə-\ *adj* — **val-ue-less-ness** *n*

value received; val-u-ing (15c) 1 a : to estimate or assign the
monetary worth of : APPRAISE ⟨~ a necklace⟩ b : to rate or scale in
goodness, importance, or general worth : EVALUATE 2 : to consider
or rate highly : PRIZE, ESTEEM ⟨~s your opinion⟩ *syn* see ESTIMATE,
APPRECIATE — **val-u-er** \-yə-wər\ *n*

value added tax *n* (1935) : an incremental excise that is levied on the
value added at each stage of the processing of a raw material or the
production and distribution of a commodity and that typically has the
impact of a sales tax on the ultimate consumer

valued \ˈval-(ˌ)yüd, -yədˇ\ *adj* (1595) : having a value or values esp. of a
specified kind or number — often used in combination ⟨real-*valued*⟩

value-free \ˈval-(ˌ)yü-ˈfrē\ *adj* (1948) : making or having no value
judgments ⟨~ distinctions⟩ ⟨~ economics⟩

value judgment *n* (1899) : a judgment assigning a value (as good or
bad) to something

va-lu-ta \və-ˈlü-tə, -(ˌ)tä\ *n* [It, value, fr. (assumed) VL *valuta*] (1920)
1 : the agreed upon or exchange value of a currency 2 : FOREIGN EX-
CHANGE 2

val-vate \ˈval-ˌvāt\ *adj* (1829) : having valves or parts resembling a
valve; *esp* : meeting at the edges without overlapping in the bud (as in
the calyx of a mallow)

valve \ˈvalv\ *n* [L *valva*; akin to L *volvere* to roll — more at VOLUBLE]
(14c) 1 *archaic* : a leaf of a folding or double door 2 [NL *valva*, fr.
L] : a structure esp. in a vein or lymphatic that closes temporarily a
passage or orifice or permits movement of fluid in one direction only 3
a : any of numerous mechanical devices by which the flow of liquid,
gas, or loose material in bulk may be started, stopped, or regulated by
a movable part that opens, shuts, or partially obstructs one or more
ports or passageways; *also* : the movable part of such a device b : a
device in a brass instrument for quickly channeling air flow through an
added length of tube in order to change the fundamental tone by some
definite interval c *chiefly Brit* : ELECTRON TUBE 4 [NL *valva*, fr. L]
: one of the distinct and usu. movably articulated pieces of which the
shell of some shell-bearing animals (as lamellibranch mollusks, bra-
chiopods, and barnacles) consists 5 [NL *valva*, fr. L] a : one of the
segments or pieces into which a dehiscing capsule or legume separates
b : the portion of various anthers (as of the barberry) resembling a lid
c : one of the two encasing membranes of a diatom — **valved** \ˈvalvdˇ\
adj — **valve·less** \ˈvalv-ləs\ *adj*

val-vu-la \ˈval-vyə-lə\ *n, pl* **-lae** \-ˌlē, -ˌlī\ [NL, dim. of L *valva*] (1615)
: a small valve or fold

val-vu-lar \ˈval-vyə-lər\ *adj* (1797) 1 : resembling or functioning as a
valve; *also* : opening by valves 2 : of, relating to, or affecting a valve
esp. of the heart ⟨~ heart disease⟩

val-vu-li-tis \ˌval-vyə-ˈlī-təs\ *n* [NL] (ca. 1891) : inflammation of a
valve esp. of the heart

va-moose \və-ˈmüs, və-\ *vi* **va-moosed; va-moos-ing** [Sp *vamos* let us
go, suppletive 1st pl. imper. (fr. L *vadere* to go) of *ir* to go, fr. L *ire* —
more at WADE, ISSUE] (1840) : to depart quickly

¹vamp \ˈvamp\ *vb* [*¹vamp*] *vt* (1599) 1 a : to provide (a shoe) with a
new vamp b : to piece (something old) with a new part : PATCH ⟨~ up
old sermons⟩ 2 : INVENT, FABRICATE ⟨~ up an excuse⟩ ~ *vi* : to play
a musical vamp — **vamp·er** *n*

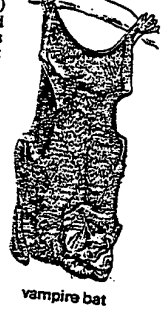
²vamp *n* [ME *vampe* sock, fr. OF *avantpié*, fr. *avant-* fore- + *pié* foot, fr.
L *ped-*, *pes* — more at VANGUARD, FOOT] (1654) 1 : the part of a shoe
upper or boot upper covering esp. the forepart of the foot and some-
times also extending forward over the toe or backward to the back
seam of the upper 2 [*¹vamp*] : a short introductory musical passage
often repeated several times (as in vaudeville) before a solo or between
verses

³vamp *n* [short for *vampire*] (ca. 1911) : a woman who uses her charm
or wiles to seduce and exploit men — **vamp·ish** \ˈvam-pish\ *adj*

⁴vamp *vt* (ca. 1915) : to practice seductive wiles on

vam·pire \ˈvam-ˌpīr\ *n* [F, fr. G *Vampir*, fr. Serbo-Croatian *vampir*]
(1734) 1 : the reanimated body of a dead person believed to come
from the grave at night and suck the blood of persons asleep 2 a
: one who lives by preying on others b : a woman who exploits and
ruins her lover 3 : VAMPIRE BAT — **vam·pir·ish** \-ish\ *adj*

vampire bat *n* (1790) : any of several Central and
So. American bats (*Desmodus rotundus*, *Diaemus
youngi*, and *Diphylla ecaudata* of the subfamily
Desmodontinae of the family Phyllostomidae)
that feed on the blood of birds and mammals and
esp. domestic animals and that are sometimes
vectors of equine trypanosomiasis and of rabies;
also : any of several other bats (as of the families
Megadermatidae and Phyllostomidae) that do
not feed on blood but are sometimes reputed to
do so



vampire bat

vam·pir·ism \-ˌpīr-ˌi-zəm\ *n* (1794) 1 : belief in
vampires 2 : the actions of a vampire

¹van \ˈvan\ *n* [ME, fr. MF, fr. L *vannus* — more
at WINNOW] (14c) 1 *dial Eng* : a winnowing
device (as a fan) 2 : WING 1a

²van *n* [by shortening] (1610) : VANGUARD

³van *n* [short for *caravan*] (1829) 1 a : a usu.
enclosed wagon or motortruck used for transpor-
tation of goods or animals; *also* : CARAVAN 2a b
: a multipurpose enclosed motor vehicle having a
boxlike shape, rear or side doors, and side panels
often with windows c : a detachable passenger
cabin transportable by aircraft or truck 2 *chiefly Brit* : an enclosed
railroad freight or baggage car

⁴van *vt* **vanned; van·ning** (1840) : to transport by van

va·na·date \ˈva-nə-ˌdāt\ *n* [NL *vanadium* + E *¹-ate*] (1835) : a salt
derived from vanadium pentoxide and containing pentavalent vana-
dium

va·na·di·um \və-ˈnā-dē-əm\ *n* [NL, fr. ON *Vanadis* Freya] (1833) : a
grayish malleable ductile metallic element found combined in minerals
and used esp. to form alloys (as vanadium steel) — see ELEMENT table

vanadium pentoxide *n* (1885) : a yellowish red crystalline compound
V_2O_5 used esp. in glass manufacture and as a catalyst

Van Al·len belt \van-ˈa-lən-\ *n* [James A. *Van Allen*] (1958) : a belt of
intense radiation in the magnetosphere composed of energetic charged
particles trapped by the earth's magnetic field; *also* : a similar belt
surrounding another planet

va·nas·pa·ti \və-ˈnəs-pə-tē, -ˈnäs-\ *n* [Skt, forest tree, soma plant, lit.,
lord of the forest, fr. *vana* forest + *pati* lord, master — more at PO-
TENT] (1941) : a hydrogenated vegetable fat used as a butter substitute
in India

van·dal \ˈvan-dᵊlˇ\ *n* [L *Vandalii* (pl.), of Gmc origin] (1555) 1 *cap* : a
member of a Germanic people who lived in the area south of the Baltic

Abstract

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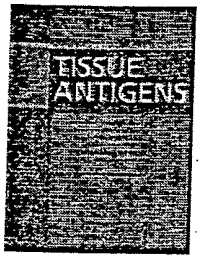
The HLA Dictionary 2001: a summary of HLA-A, -B, -C, -DRB1/3/4/5, -DQB1 alleles and their association with serologically defined HLA-A, -B, -C, -DR and -DQ antigens



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Abstract: This report presents the serologic equivalents of 123 HLA-A, 272 HLA-B and 155 HLA-DRB1 alleles. The equivalents cover over 64% of the presently identified HLA-A, -B and -DRB1 alleles. The dictionary is an update of the one published in 1999 and also includes equivalents for HLA-C, DRB3, DRB4, DRB5 and DQB1 alleles. The data summarize information obtained by the WHO Nomenclature Committee for Factors of the HLA System, the International Cell Exchange (UCLA), the National Marrow Donor Program (NMDP) and individual laboratories. In addition, a listing is provided of alleles which are expressed as antigens with serologic reaction patterns that differ from the well-established HLA specificities. The equivalents provided will be useful in guiding searches for unrelated hematopoietic stem cell donors in which patients and/or potential donors are typed by either serology or DNA-based methods. These equivalents will also serve typing and matching procedures for organ transplant programs where HLA typings from donors and from recipients on waiting lists represent mixtures of serologic and molecular typings. The tables with HLA equivalents and a questionnaire for submission of serologic reaction patterns for poorly identified allelic products will also be available on the WMDA web page: http://www.worldmarrow.org.

Affiliations
World Marrow Donor Association Quality Assurance Working Group, Leiden, The Netherlands,WHO Nomenclature Committee for Factors of the HLA System,International Cell